UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,669	12/21/2001	Rama Akella	SBI-111	1708

7590 06/10/2004

KENNETH S. BARROW
CENTERPULSE USA INC.
12 E GREENWAY PLAZA
SUITE 1000
HOUSTON, TX 77046-1203

EXAMINER	
RUSSEL, JEFFREY E	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 06/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/027,669	AKELLA ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *13-15,20-29 and 32-36* is/are allowed.

6)☒ Claim(s) *1-12,16-19,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12, 16-19, 30, and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no original disclosure supporting the limitation that angiogenesis is promoted without induction of osteogenesis, as is recited in instant claims 1, 12, 16, 30, and 31. There is no literal recitation of the limitation in the original disclosure of the application. The limitation also does not appear to be inherently disclosed in the application as originally filed, especially in view of the original disclosure of bone morphogenetic proteins as possible growth factors (see, e.g., page 6, line 4, and originally-filed claim 12). Applicants point to page 17, lines 8-9; Figures 1-3; and page 7, lines 15-19; as support for the new claim limitation. However, none of these mention osteogenesis. While page 17, lines 8-9, and the figures disclose that a control experiment results in cartilage formation, the specification does not make any connection between cartilage formation and osteogenesis. The disclosure at page 7, lines 15-19, is fully consistent with the disclosure of the Chinese Patent 1,163,780, applied below, which teaches that capillary formation, i.e. new blood flow, is a major step in bone induction. Silence in the disclosure concerning osteogenesis does not constitute support for a positive statement that osteogenesis does not occur. See Ex parte Grasselli, 231 USPQ 393, aff'd on reconsideration 231 USPQ 395 (BPAI 1983). The specification does not show in "full, clear, concise, and exact

terms" that Applicants contemplated and had within their possession compositions which promoted angiogenesis without inducing osteogenesis. 2. Claims 1-12, 16-19, 30, and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear how the phrase "capable of promoting angiogenesis without inducing osteogenesis" at claim 1, lines 4-5, should be interpreted. In particular, it is not clear if this means a composition needs only to be capable of promoting angiogenesis with osteogenesis at one site in a living subject in order to be embraced by the claim, or if the limitation means that the claimed compositions are incapable of inducing osteogenesis at any site in any living subject. This difference in interpretation is emphasized by dependent claim 12, which recites that the polypeptide is a bone morphogenetic protein, which presumably is capable of inducing osteogenesis at least at or near a pre-existing site of bone or cartilage in a living subject. Given that Applicants disclose bone morphogenetic proteins as potential polypeptides of the TGF-β superfamily, it is also not clear if this phrase, which also occurs in various forms in claims 16, 30, and 31, acts as a functional limitation excluding bone morphogenetic proteins, and other polypeptides of the TGF-β superfamily having osteogeneic activities such as the bFGF of the Chinese Patent 1,163,780, from the claimed compositions and methods.

3. Claim 12 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Independent claim 1 has been amended to require that the claimed compositions be capable of promoting angiogenesis without inducing osteogenesis. However,

dependent claim 12 requires the presence of bone morphogenetic proteins, which possess the function of inducing osteogenesis. Accordingly, claim 12 does not appear to be embraced within the scope of the independent claim.

4. The effective filing date of instant claims 1-12, 16-18, 30, and 31 is deemed to be December 21, 2001, the filing date of the instant application. Instant claims 1-12, 16-18, 30, and 31 are not deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing date of parent application 09/748,038 because the parent application, under the test of 35 U.S.C. 112, first paragraph, does not disclose the genus of TGF-β superfamily polypeptides; does not disclose vinyl pyrrolidone polymers in general; does not disclose the molecular weight range of about 2.5 kD to about 20 kD; does not disclose water or aqueous buffer solutions as solvents for the growth factor composition; does not disclose the polymer concentration range of about 0.1% w/v to about 70% w/v or the narrower ranges of instant claims 8-10; does not disclose promoting soft tissue regeneration in general; and does not disclose increasing the bioavailability of growth factors.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being obvious over the Chinese Patent 1,163,780. The Chinese Patent '780 teaches forming an aqueous solution of bone morphogenetic protein and combining it with a second aqueous solution of bFGF and PVP. The resultant composition is used for osteogenesis stimulation, i.e. is used to generate cartilage and bone tissue. The bFGF in the composition stimulates capillary formation inside cartilage, which is a major step in the formation of bone by bone induction. The PVP acts to solubilize both the

bone morphogenetic protein and the bFGF so that a complete suspension can be prepared. In in vivo testing, the composition is administered by injection. See, e.g., page 2; page 4, lines 10-12; page 8, lines 13-23; and page 11, lines 7-13; of the translation. The cartilage whose growth is stimulated by the composition of the Chinese Patent '780 is a soft tissue. Because the second aqueous solution of the Chinese Patent '780 comprises bFGF which stimulates capillary formation, the composition is capable of promoting angiogenesis. Because the components of the second aqueous solution of the Chinese Patent '780, i.e. the bFGF and the PVP, are the same as the components recited in Applicant's claimed composition, the second aqueous solution of the Chinese Patent '780 is deemed to be inherently capable of promoting angiogenesis without inducing osteogenesis to the same extent claimed by Applicants. Note that although the Chinese Patent '780 intends to use its composition to stimulate osteogenesis, this does not mean that the composition can not be applied to some site in some subject so that angiogenesis without osteogenesis occurs. A difference in intended uses does not automatically impart patentability to product-by-process claims. The Chinese Patent '780 does not teach a molecular weight or solution concentration for its PVP. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine a molecular weight and solution concentration for the PVP of the Chinese Patent '780 because molecular weight and solution concentration are art-recognized result-effective variables which are routinely determined and optimized in the polymer, solution chemistry, and pharmaceutical arts.

7. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being obvious over the Chinese Patent 1,163,780 as applied against claims 1-12 above, and further in view of the Robinson et al text (Reference C8 of the Information Disclosure Statement filed October 22, 2003). As noted

above, although the Chinese Patent '780 does not teach a molecular weight for its PVP, the Robinson et al text teaches that typical molecular weights for injectable human preparations are 12, 15, 17, and 30 kDa. See page 10, last paragraph. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine a molecular weight for the PVP of the Chinese Patent '780 from within the range of molecular weights taught by the Robinson et al text because molecular weight is an art-recognized result-effective variable which is routinely determined and optimized in the pharmaceutical arts as shown by the Robinson et al text.

8. Applicant's arguments filed May 7, 2004 have been fully considered but they are not persuasive.

The rejections of method claims 16-18, 30, and 31 over the Chinese Patent 1,163,780 as the primary reference are withdrawn in view of the new claim limitations requiring that angiogenesis be induced without induction of osteogenesis. The Chinese patent '780 requires the induction of angiogenesis.

Claims 1-12 remain rejected over the Chinese Patent '780, optionally in combination with the Robinson et al text. These prior art rejections are dependent upon resolution of the claim interpretation issue addressed in the above rejection under 35 U.S.C. 112, second paragraph. If Applicants' claim language should be interpreted as prohibiting the claimed compositions from having osteogenesis inducing properties under any circumstances, then the prior art rejections should be withdrawn. If Applicants' claim language should be interpreted as merely requiring that there be at least one site in one living subject where the claimed composition induces angiogenesis without inducing osteogenesis, then there is deemed to be

sufficient similarity between the components present in the second aqueous solution of the Chinese Patent '780 and the components present in Applicants' claimed compositions to conclude that this property is inherent in the second aqueous solution of the Chinese Patent '780.

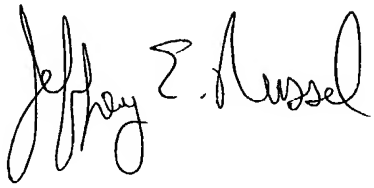
9. Claims 13-15, 20-29, and 32-36 are allowed. Claim 19 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, first and second paragraphs, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (571) 272-0961. The fax number for formal communications to be entered into the record is (703) 872-9306; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

June 7, 2004